Long-term safety and efficacy outcomes following conversion to eslicarbazepine acetate (ESL) monotherapy in patients with partial-onset seizures (POS): a post-HOC subgroup analysis of patients who continued to receive ESL as monotherapy for up to 12 months

Steve Chung, 1 Saurabh R Sinha, 2 Asathi Shah, 3 John Stern, 4 Hailong Cheng, 5 Todd Grinnell, 6 David Blum 7

1Barrow University Medical Center, Phoenix, AZ, USA; 2Department of Neurology, Duke University Medical Center, Durham, NC, USA; 3Wayne State University, Detroit Medical Center, Detroit, MI, USA; 4Department of Neurology, Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA; 5Sarvon Pharmaceuticals Inc., Marlborough, MA, USA

INTRODUCTION

Eslicarbazepine acetate (ESL) is a once-daily oral antiepileptic drug (AED) for the treatment of partial-onset seizures (POS).

Data from two identical Phase III, conversion-to-ESL monotherapy trials (093-045 and 093-046) showed that conversion to ESL monotherapy was effective and safe in adult patients with POS who were well-controlled on one trial monotherapy.

The proportion of patients who failed the trial (i.e., those not maintain well-controlled seizures at 16 weeks) was less than the proportion that failed the historical control studies (ESL monotherapy was therefore subject to superiority in the historical control).

In this post-HOC analysis, patients who were in the open-label extension (OLE) of the two trial studies (093-045 and 093-046), remained in active control during studies 045 and 046 were maintained on long-term treatment with ESL, and no evidence of uncontrolled seizures were identified.

A total of 393 patients received ESL monotherapy (closed dose: 1300 mg or 1350 mg q2d for 10 weeks after 3-week placebo period in studies 045 and 046). The post HOC analysis included 270 patients (69.3%) from the entire study 045/046 population. – ESL monotherapy was considered to start when the last baseline AED was stopped, i.e. At Week 0 of the post-HOC period.

This report describes a post-hoc analysis of outcomes from studies 045, 046 and 050 for the time period when patients were taking ESL as a monotherapy i.e., they had not added any other AEDs, this patient population was defined as the ‘true ESL monotherapy’ subgroup.

OBJECTIVES

• To evaluate long-term safety and efficacy outcomes in adults with POS who continued to receive ESL as monotherapy.

METHODS

Studies 045 and 046

Studies (NCT01789797 & NCT01798513) were 10-week, single-blind, randomized, Phase III, conversion-to-monotherapy studies, which assessed the efficacy of 1000 mg and 1200 mg ESL versus a historical control as described by French at al. 1

Patients aged ≥15-67 years with POS were randomized to either ESL (closed dose at 1300 mg or 1350 mg q2d) or placebo (standardized frequency assessment [SFA] [both n = 28 days] were randomized 1:1) to receive ESL 1300 mg or 1350 mg q2d for 10 weeks after a 3-week washout period.

The designs of studies 045 and 046 are shown in Figure 5.

Post-hoc analysis

The post-hoc analysis was undertaken to assess the safety and efficacy outcomes in patients who received ESL monotherapy during double-blind trials (045, 046, 050) and for the remainder of the 12-month open-label extension (OLE) period.

– ESL monotherapy was considered to start when the last baseline AED was stopped, i.e. At Week 0 of the post-HOC period.

• The ‘true ESL monotherapy’ safety population included all patients who were treated at least once with ESL and completed the ESL monotherapy period. i.e., Those enrolled in the 12-week monotherapy period.

The evaluation period began at the start of the 10-week ESL monotherapy period and ended either:

– When a non-ESL AED was added, or
– When study participation ended, or
– On March 31, 2014 data cut-off for the patients who enrolled in study 050.

The ‘true ESL monotherapy’ efficacy population included patients who completed the AED conversion in ESL monotherapy, remained in active control during the 3-week titration period, and had at least one recurrent seizure assessment during ESL before the March 14, 2014 data cut-off.

RESULTS

Patients

The ‘true ESL monotherapy’ safety and efficacy populations consisted of 273 and 240 patients, respectively.

The demographics and baseline characteristics of patients in the ‘true ESL monotherapy’ subgroup are shown in Table 1.

Exposure

Table 3.

<table>
<thead>
<tr>
<th>Variable</th>
<th>ESL monotherapy subgroup n = 270</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment duration</td>
<td>547 days (1 to 2100)</td>
</tr>
<tr>
<td>Days on treatment</td>
<td>45 (1 to 1050)</td>
</tr>
<tr>
<td>Days with treatment</td>
<td>45 (1 to 1050)</td>
</tr>
</tbody>
</table>

Conclusions

At the time of cut-off, 52.7% of patients who had entered the OLE study were continuing to take ESL as monotherapy, without other AEDs.

Safety outcomes in this true ESL monotherapy subgroup were generally consistent with those reported for the overall study population and those of the Phase III conversion-to-ESL monotherapy trials. 

The incidence of AEs (≥3%) and TEAEs (≥1%) leading to discontinuation of ESL in the ‘true ESL monotherapy’ subgroup were lower than reported for the total population of the 03 study (10.6% and 8.4%, respectively).

The long-term exposure of up to 12 months was comparable with the true ESL monotherapy and the total study population:

– Median exposure in SFA from baseline was 888 vs 886.1%
– 50% responder rate: 63.3% vs 62.5%.

REFERENCES


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AED: antiepileptic drug; ESL: eslicarbazepine acetate; ITT: intent-to-treat; TEAE: treatment-emergent adverse event.